（書式１８）

学　位　論　文　要　約
（　Ａｂｓｔｒａｃｔ）

博士論文題目 Title of dissertation

Contribution of different evolutionary patterns to human sapovirus intra-host diversity

（ヒトサポウイルスの進化様式の違いがもたらす宿主内遺伝的多様性への影響）

東北大学大学院医学系研究科　　専攻

病理病態学　講座　　微生物学分野

学籍番号（＊論文博士は受付番号）Student Number B6MD5139 氏名 Name Kagning Tsinda Emmanuel

Background: The human sapovirus is an important cause of both sporadic acute diarrhea and gastroenteritis outbreaks especially in developing countries. All age groups are affected, but children under five years of age incur the highest burden of disease. Several studies have described sapovirus epidemiology, but little is known regarding the novel GII.8 genotype and the sapovirus inter-genotype evolution over time.

Method: In the first part of my research works, I sequenced a novel sapovirus GII.8 genotype detected in two fecal samples collected during a Peruvian birth cohort study conducted between June 2007 and May 2010. Sapovirus was detected by quantitative reverse transcriptase PCR, genotyped based on the sequence of the partial capsid gene and overlapping amplicons spanning the near complete genome were sequenced by sanger sequencing.

In the second part of this research, I analyzed sapovirus intergenotype evolutionary patterns. I retrieved and analyzed 277 sapovirus full capsid data from GenBank repository. I computed the capsid protein genetic distances and the isolation date differences. I found that there are different evolutionary patterns between genotype GI.1 and GI.2. I sequenced sapovirus GI.1 and GI.2 detected in fecal samples from infected Peruvian and Japanese individuals. nine GI.1 and eleven GI.2 positive fecal samples from a 2016-2018 Peruvian birth-cohort study were selected by convenience sampling and processed to describe sapovirus mutations within-host mutations. In addition, GI.1 and GI.2 fecal samples which tested positive the during 2013/2015 sapovirus outbreaks in Miyagi prefecture (Japan) were processed to describe the inter-host host mutations of sapovirus. Sapovirus genomes were sequenced using a multiplex amplicon next generation sequencing method.

Results: In this dissertation, I described the sapovirus GII.8 near complete genome sequence, which has been useful to

detect and characterize sapovirus GII.8 strains circulating in other parts of the world. Also, I found that compared to GI.1, sapovirus GI.2 accumulate intra-host mutations two times faster. Genetic diversity, selective pressure, capsid mutations and polymerase mutations were significantly associated with sapovirus inter-genotype evolutionary patterns. My findings clarify possible mechanisms that drive sapovirus GI.2 global emergence and adaptation as sapovirus GI.2 became the first cause of sapovirus outbreaks worldwide. The complex interrelations between sapovirus genotype evolution patterns, selective pressure, genetic diversity, and mutation frequency indicates that further studies are needed to better characterize effects of GI.2 antigenic changes on the virus stability, epidemiology, and virulence.